



## SEQUENCE LISTING

<110> Anderson, John P.  
Basi, Guriqbal  
Doane, Minh Tam  
Frigon, Normand  
John, Varghese  
Power, Michael  
Sinha, Sukanto  
Tatsuno, Gwen  
Tung, Jay  
Wang, Shuwen  
McConlogue, Lisa

<120> Beta-Secretase Enzyme Compositions and  
Methods

<130> 228-US-NEW2C6

<140> US 09/724,569

<141> 2000-11-28

<150> US 09/501,708

<151> 2000-02-10

<150> 60/119,571

<151> 1999-02-10

<150> 60/139,172

<151> 1999-06-15

<160> 104

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09724563 071701

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Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
      435              440              445
Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
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Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
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<220>

<223> Degenerate oligonucleotide primer derived from SEQ  
 ID NO: 2

<400> 18  
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23

<210> 19  
 <211> 20  
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 <213> Artificial Sequence

<220>

<223> Degenerate oligonucleotide primer derived from SEQ  
 ID NO: 2

<400> 19  
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20

<210> 20  
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 ID NO: 2

<400> 20  
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26

<210> 21  
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 ID NO: 2

<400> 21  
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<210> 22  
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<210> 27

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<212> DNA

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<221> misc\_feature

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<210> 28

<211> 17

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<223> n = A,T,C or G

<400> 28

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<210> 35  
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<210> 40  
 <211> 26  
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<400> 40  
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<210> 41  
 <211> 26  
 <212> DNA  
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<220>  
 <223> Degenerate oligonucleotide primer

<400> 41  
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<210> 42  
 <211> 2348  
 <212> DNA  
 <213> Homo sapiens

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<212> PRT
<213> Homo sapiens

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 20          25          30
Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp
 35          40          45
Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
 50          55          60
His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
 65          70          75          80
Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
 85          90          95
Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
100          105          110
Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
115          120          125
Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
130          135          140
Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
145          150          155          160
His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
165          170          175
Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
180          185          190
Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
195          200          205
Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
210          215          220
Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
225          230          235          240
Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val
245          250          255
Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys
260          265          270
Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala
275          280          285
Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
290          295          300
Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
305          310          315          320
Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
325          330          335
Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
340          345          350
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 Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe  
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 <212> DNA  
 <213> Homo sapiens

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<212> PRT  
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<220>  
<223> Flag sequence

<400> 45  
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<210> 46  
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<212> PRT  
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<400> 46  
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<210> 47  
<211> 23  
<212> PRT  
<213> Homo sapiens

<400> 47  
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<210> 48  
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<221> misc\_feature  
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aggctcgcaa	catcttcttc	tggaggccgt	ggttggcggg	tatggagcag	cagacgcgct	15300
acttcgagcg	gaggcatccg	gagcttgcat	gatcgcccg	gctccggcg	tatatgtctc	15360
gcattggtct	tgaccaactc	tatcagagct	tggttgacgg	caatttcgat	gatgcagctt	15420
gggcgcgagg	tcgatgcgac	gcaatcgtcc	cgtccggagc	cgggactgtc	gggcgtacac	15480
aaatcgccc	cagaagcgcg	ccgtcttgga	ccgatggctg	tgtagaagta	ctcgccgata	15540
gtggaaacgg	gagatggggg	aggctaactg	aaacacggaa	ggagacaata	ccggaaggaa	15600

```

cccgcgctat gacggcaata aaaagacaga ataaaacgca cgggtgttgg gtcgtttgtt 15660
cataaacgcg ggggttcggtc ccagggtctg cactctgtcg ataccccacc gagaccccat 15720
tggggccaat acgcccgcgt ttcttccttt tccccacccc acccccacag ttcgggtgaa 15780
ggcccagggc tcgcagccaa cgtcggggcg gcaggccctg ccatagccac tggccccgtg 15840
ggttagggaac ggggtccccc atggggaatg gtttatgggt cgtgggggtt attattttgg 15900
gcgttgctgt ggggtctggtc cacgactgga ctgagcagac agacccatgg tttttggatg 15960
gcctgggcat ggaccgcatg tactggcgcg acacgaacac cgggcgtctg tggctgccaa 16020
acacccccga cccccaaaaa ccaccgcgcg gatttctggc gtgccaagct agtcgaccaa 16080

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<210> 49
<211> 32
<212> DNA
<213> Homo sapiens

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<400> 49
cccggccgga ggggcagctt tgtggagatg gt 32

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```

<210> 50
<211> 11
<212> PRT
<213> Homo sapiens

```

```

<400> 50
Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
1             5             10

```

```

<210> 51
<211> 5
<212> PRT
<213> Homo sapiens

```

```

<400> 51
Val Asn Leu Asp Ala
1             5

```

```

<210> 52
<211> 9
<212> PRT
<213> Artificial Sequence

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```

<220>
<223> Synthetic oligopeptide substrate

```

```

<400> 52
Ser Glu Val Asn Leu Asp Ala Glu Phe
1             5

```

```

<210> 53
<211> 30
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> Synthetic oligopeptide substrate

```

```

<400> 53
Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile
1             5             10             15

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Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe  
                   20                                  25                                  30

<210> 54

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<223> Wild type Amyloid Precursor Protein cleavage site  
          (fragment)

<400> 54

Val Lys Met Asp Ala  
   1                                  5

<210> 55

<211> 24

<212> PRT

<213> Homo sapiens

<400> 55

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
   1                                  5                                  10                                  15  
 Glu Met Val Asp Asn Leu Arg Gly  
                                   20

<210> 56

<211> 15

<212> PRT

<213> Homo sapiens

<400> 56

Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg  
   1                                  5                                  10                                  15

<210> 57

<211> 419

<212> PRT

<213> Homo sapiens

<400> 57

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
   1                                  5                                  10                                  15  
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
                                   20                                  25                                  30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
                                   35                                  40                                  45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
                                   50                                  55                                  60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
  65                                  70                                  75                                  80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
                                   85                                  90                                  95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
                                   100                                  105                                  110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
                                   115                                  120                                  125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
                                   130                                  135                                  140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile

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145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 Glu Gly Ile Leu Glu Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 Val Ser Ala

<210> 58  
 <211> 407  
 <212> PRT  
 <213> Homo sapiens

<400> 58  
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
 1 5 10 15  
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
 20 25 30  
 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
 35 40 45  
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
 50 55 60  
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
 65 70 75 80  
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
 85 90 95  
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
 100 105 110  
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
 115 120 125  
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
 130 135 140  
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr

145                      150                      155                      160  
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
                                  165                      170                      175  
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
                                  180                      185                      190  
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
                                  195                      200                      205  
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
                                  210                      215                      220  
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
                                  225                      230                      235                      240  
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
                                  245                      250                      255  
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys  
                                  260                      265                      270  
 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala  
                                  275                      280                      285  
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met  
                                  290                      295                      300  
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln  
                                  305                      310                      315                      320  
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
                                  325                      330                      335  
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
                                  340                      345                      350  
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
                                  355                      360                      365  
 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala  
                                  370                      375                      380  
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr  
                                  385                      390                      395                      400  
 Asn Ile Pro Gln Thr Asp Glu  
                                  405

<210> 59  
 <211> 452  
 <212> PRT  
 <213> Homo sapiens

<400> 59  
 Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
   1                                 5                                 10                                 15  
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
                                  20                                 25                                 30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
                                  35                                 40                                 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
                                  50                                 55                                 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
   65                                 70                                 75                                 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
                                  85                                 90                                 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
                                  100                                 105                                 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
                                  115                                 120                                 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
                                  130                                 135                                 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
   145                                 150                                 155                                 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp

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165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
 420 425 430  
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
 435 440 445  
 Gln Thr Asp Glu  
 450

<210> 60  
 <211> 420  
 <212> PRT  
 <213> Homo sapiens

<400> 60

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
 1 5 10 15  
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
 20 25 30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp

130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys  
 420

<210> 61

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic peptide inhibitor

<221> MOD\_RES

<222> 4

<223> Xaa = hydroxyethylene

<400> 61

Glu Val Met Xaa Ala Glu Phe

1

5

<210> 62

<211> 26

<212> PRT

<213> Homo sapiens

<400> 62

Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met

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1 5 10 15  
 Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
 20 25

<210> 63  
 <211> 33  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> P26-P4'sw peptide substrate

<400> 63  
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
 1 5 10 15  
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu  
 20 25 30  
 Phe

<210> 64  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <223> P26-P1' peptide substrate with CGG linker

<400> 64  
 Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
 1 5 10 15  
 Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu  
 20 25

<210> 65  
 <211> 501  
 <212> PRT  
 <213> Mus musculus

<400> 65  
 Met Ala Pro Ala Leu His Trp Leu Leu Leu Trp Val Gly Ser Gly Met  
 1 5 10 15  
 Leu Pro Ala Gln Gly Thr His Leu Gly Ile Arg Leu Pro Leu Arg Ser  
 20 25 30  
 Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp

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165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro  
 195 200 205  
 Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
 420 425 430  
 Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
 435 440 445  
 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala  
 450 455 460  
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
 465 470 475 480  
 Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Gly Asp Asp  
 485 490 495  
 Ile Ser Leu Leu Lys  
 500

&lt;210&gt; 66

&lt;211&gt; 480

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 66

Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala  
 1 5 10 15  
 Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
 20 25 30  
 Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
 35 40 45  
 Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
 50 55 60  
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
 65 70 75 80  
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu

				85				90					95				
Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr		
			100					105					110				
Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro		
		115					120					125					
His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu		
		130				135					140						
Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly		
145					150					155					160		
Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe		
				165					170					175			
Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu		
			180					185					190				
Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala		
		195					200					205					
Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr		
		210				215					220						
Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu		
225					230					235					240		
Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp		
				245					250					255			
Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr		
			260					265					270				
Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala	Ala	Val	Lys	Ser	Ile		
		275					280					285					
Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly		
		290					295				300						
Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe		
305					310					315					320		
Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe		
				325					330					335			
Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val		
			340					345					350				
Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys	Phe	Ala	Ile	Ser	Gln	Ser	Ser		
		355					360					365					
Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile	Met	Glu	Gly	Phe	Tyr	Val	Val		
						375					380						
Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly	Phe	Ala	Val	Ser	Ala	Cys	His		
385					390					395					400		
Val	His	Asp	Glu	Phe	Arg	Thr	Ala	Ala	Val	Glu	Gly	Pro	Phe	Val	Thr		
				405					410					415			
Leu	Asp	Met	Glu	Asp	Cys	Gly	Tyr	Asn	Ile	Pro	Gln	Thr	Asp	Glu	Ser		
			420					425					430				
Thr	Leu	Met	Thr	Ile	Ala	Tyr	Val	Met	Ala	Ala	Ile	Cys	Ala	Leu	Phe		
		435					440					445					
Met	Leu	Pro	Leu	Cys	Leu	Met	Val	Cys	Gln	Trp	Arg	Cys	Leu	Arg	Cys		
		450				455					460						
Leu	Arg	Gln	Gln	His	Asp	Asp	Phe	Ala	Asp	Asp	Ile	Ser	Leu	Leu	Lys		
465					470					475					480		

&lt;210&gt; 67

&lt;211&gt; 444

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 67

Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln		
1				5				10						15			
Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn		
			20					25					30				

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<210> 68
<211> 395
<212> PRT
<213> Homo sapiens
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<400> 68  
Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln  
1 5 10 15

Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
                   20                  25                  30  
 Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
                   35                  40                  45  
 His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
                   50                  55                  60  
 Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
                   65                  70                  75                  80  
 Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
                   85                  90                  95  
 Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
                   100                  105                  110  
 Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
                   115                  120                  125  
 Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
                   130                  135                  140  
 Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
                   145                  150                  155                  160  
 Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
                   165                  170                  175  
 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
                   180                  185                  190  
 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
                   195                  200                  205  
 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
                   210                  215                  220  
 Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
                   225                  230                  235                  240  
 Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
                   245                  250                  255  
 Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val  
                   260                  265                  270  
 Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
                   275                  280                  285  
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
                   290                  295                  300  
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
                   305                  310                  315                  320  
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
                   325                  330                  335  
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
                   340                  345                  350  
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
                   355                  360                  365  
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
                   370                  375                  380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
                   385                  390                  395

&lt;210&gt; 69

&lt;211&gt; 439

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 69

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
                   1                  5                  10                  15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
                   20                  25                  30  
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
                   35                  40                  45

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Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
 50 55 60  
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
 65 70 75 80  
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
 85 90 95  
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
 100 105 110  
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
 115 120 125  
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
 130 135 140  
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
 145 150 155 160  
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
 165 170 175  
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
 180 185 190  
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
 195 200 205  
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser  
 210 215 220  
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe  
 225 230 235 240  
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe  
 245 250 255  
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly  
 260 265 270  
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly  
 275 280 285  
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr  
 290 295 300  
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
 305 310 315 320  
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
 325 330 335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
 340 345 350  
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
 355 360 365  
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
 370 375 380  
 Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met  
 385 390 395 400  
 Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys  
 405 410 415  
 Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala  
 420 425 430  
 Asp Asp Ile Ser Leu Leu Lys  
 435

&lt;210&gt; 70

&lt;211&gt; 390

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 70

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
 20 25 30

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His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
 65 70 75 80  
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
 85 90 95  
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
 100 105 110  
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
 115 120 125  
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
 130 135 140  
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
 145 150 155 160  
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
 165 170 175  
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
 180 185 190  
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
 195 200 205  
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
 210 215 220  
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
 225 230 235 240  
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
 245 250 255  
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys  
 260 265 270  
 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala  
 275 280 285  
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met  
 290 295 300  
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln  
 305 310 315 320  
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
 325 330 335  
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
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 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
 355 360 365  
 Gly Phe Ala Val Ser Ala  
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<210> 72

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> P10-P4'staD-V peptide inhibitor

<221> MOD\_RES

<222> 10

<223> Xaa is statine moiety

<400> 72

Lys Thr Glu Glu Ile Ser Glu Val Asn Xaa Val Ala Glu Phe  
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<210> 73

<211> 9

<212> PRT

<213> Artificial Sequence



&lt;220&gt;

&lt;223&gt; P4-P4'staD-V peptide inhibitor

&lt;221&gt; MOD\_RES

&lt;222&gt; 5

&lt;223&gt; Xaa is statine moiety

&lt;400&gt; 73

Ser Glu Val Asn Xaa Val Ala Glu Phe

1

5

&lt;210&gt; 74

&lt;211&gt; 431

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 74

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			20					25					30		
Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val	Asp	Asn	Leu	Arg	Gly
		35					40					45			
Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr	Val	Gly	Ser	Pro	Pro
	50					55					60				
Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser	Ser	Asn	Phe	Ala	Val
65					70					75					80
Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr	Tyr	Gln	Arg	Gln	Leu
				85					90					95	
Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val	Tyr	Val	Pro	Tyr	Thr
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Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp	Leu	Val	Ser	Ile	Pro
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His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile	Ala	Ala	Ile	Thr	Glu
	130						135				140				
Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp	Glu	Gly	Ile	Leu	Gly
145					150					155					160
Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp	Ser	Leu	Glu	Pro	Phe
			165						170					175	
Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro	Asn	Leu	Phe	Ser	Leu
			180					185					190		
Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln	Ser	Glu	Val	Leu	Ala
		195					200					205			
Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly	Gly	Ile	Asp	His	Ser	Leu	Tyr
	210					215					220				
Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg	Glu	Trp	Tyr	Tyr	Glu
225					230					235					240
Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln	Asp	Leu	Lys	Met	Asp
				245					250					255	
Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val	Asp	Ser	Gly	Thr	Thr
		260						265					270		
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		275					280					285			
Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp	Gly	Phe	Trp	Leu	Gly
	290					295					300				
Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr	Pro	Trp	Asn	Ile	Phe
305					310					315					320
Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	Thr	Asn	Gln	Ser	Phe
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Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	Pro	Val	Glu	Asp	Val

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<210> 75
<211> 361
<212> PRT
<213> Homo sapiens
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			20					25					30		
Gly	Ser	Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His
			35				40					45			
Arg	Tyr	Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys
	50					55					60				
Gly	Val	Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly
65				70						75				80	
Thr	Asp	Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala
				85					90					95	
Asn	Ile	Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser
			100					105					110		
Asn	Trp	Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro
			115				120					125			
Asp	Asp	Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His
	130					135					140				
Val	Pro	Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu
145					150					155					160
Asn	Gln	Ser	Glu	Val	Leu	Ala	Ser	Val	Gly	Gly	Ser	Met	Ile	Ile	Gly
				165					170					175	
Gly	Ile	Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile
			180					185					190		
Arg	Arg	Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn
		195				200						205			
Gly	Gln	Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser
	210					215					220				
Ile	Val	Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe
225					230					235					240
Glu	Ala	Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe
				245					250					255	
Pro	Asp	Gly	Phe	Trp	Leu	Gly	Glu	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly
			260					265					270		
Thr	Thr	Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly
		275					280					285			
Glu	Val	Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr
	290					295					300				
Leu	Arg	Pro	Val	Glu	Asp	Val	Ala	Thr	Ser	Gln	Asp	Asp	Cys	Tyr	Lys
305					310					315					320
Phe	Ala	Ile	Ser	Gln	Ser	Ser	Thr	Gly	Thr	Val	Met	Gly	Ala	Val	Ile
				325					330					335	
Met	Glu	Gly	Phe	Tyr	Val	Val	Phe	Asp	Arg	Ala	Arg	Lys	Arg	Ile	Gly

340 345 350  
 Phe Ala Val Ser Ala Cys His Val His  
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<210> 76  
 <211> 63  
 <212> DNA  
 <213> Homo sapiens

<220>  
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 <222> (1)...(63)  
 <223> n = A,T,C or G

<400> 76  
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 aay 63

<210> 77  
 <211> 21  
 <212> PRT  
 <213> Homo sapiens

<400> 77  
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 Glu Met Val Asp Asn  
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<210> 78  
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 <212> PRT  
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<220>  
 <223> Peptide inhibitor P3-P4' XD-V  
 <221> MOD\_RES  
 <222> 3  
 <223> Xaa is hydroxyethylene or statine

<400> 78  
 Val Met Xaa Val Ala Glu Phe  
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<210> 79  
 <211> 11  
 <212> PRT  
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<400> 79  
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<210> 80  
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<220>  
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cggatcgga aacctctcga ctgttggggg gagtactccc tctcaaaagc gggcatgact      180
tctgcgctaa gattgtcagt ttccaaaaac gaggaggatt tgatattcac ctggcccgcg      240
gtgatgcctt tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca      300
agcttgaggt gtggcaggct tgagatctgg ccatacactt gagtgacaat gacatccact      360
ttgcctttct ctccacaggt gtccactccc aggtccaact gcaggtcgac tctagaccc      419

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<210> 81

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Peptide inhibitor P4-P4' XD-V

<221> MOD\_RES

<222> 4

<223> Xaa is hydroxyethylene or statine

<400> 81

Glu Val Met Xaa Val Ala Glu Phe

1 5

<210> 82

<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4' wt

<400> 82

Ser Glu Val Lys Met Asp Ala Glu Phe

1 5

<210> 83

<211> 9

<212> PRT

<213> Homo sapiens

<220>

<223> APP fragment P5-P4'wt

<400> 83

Ser Glu Val Asn Leu Asp Ala Glu Phe

1 5

<210> 84

<211> 9

<212> PRT

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<220>

<223> APP fragment

<400> 84

Ser Glu Val Lys Leu Asp Ala Glu Phe

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<220>  
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<210> 87  
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<212> PRT  
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<220>  
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<400> 87  
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<210> 88  
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<400> 88  
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<210> 89  
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<212> PRT  
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<210> 91  
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 <212> PRT  
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<210> 93  
 <211> 9  
 <212> PRT  
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<220>  
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<400> 93  
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<210> 94  
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 <212> PRT  
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<220>  
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<400> 94  
 Ser Glu Val Asn Phe Ala Ala Glu Phe  
 1 5

<210> 95

<211> 9  
 <212> PRT  
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<400> 95  
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<210> 96  
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 <212> PRT  
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<220>  
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<400> 96  
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<210> 97  
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 <212> PRT  
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<220>  
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<210> 98  
 <211> 35  
 <212> DNA  
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 <212> PRT  
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Thr Gln His Gly Ile Arg Leu Pro Leu Arg  
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 <212> PRT  
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<220>  
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<400> 101  
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 1 5

<210> 102  
 <211> 10  
 <212> PRT  
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<220>  
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<400> 102  
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 1 5 10

<210> 103  
 <211> 4  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> APP substrate fragment:WT Sequence

<400> 103  
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<210> 104  
 <211> 4  
 <212> PRT  
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<220>  
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<400> 104  
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